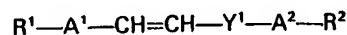


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(54) Ethylene derivatives

(57) Ethylene derivatives of the
formula:—



[wherein R¹ represents a hydroxy-
methyl or carboxy group, A¹
represents a straight-chain alkylene
group containing from 4 to 8 carbon
atoms, Y¹ represents a carbonyl or
hydroxymethylene group, A²
represents a straight- or branched-

chain alkylene group containing from
1 to 5 carbon atoms, and R²
represents a phenyl, phenoxy or
phenylthio group which may carry one
or more substituents selected from
halogen atoms, straight- or branched-
chain alkyl or alkoxy groups, each
containing from 1 to 4 carbon atoms,
and the trifluoromethyl group] and,
when R¹ represents a carboxy group,
salts thereof, are new compounds of
use in the field of mammalian
reproduction and also of use in the
control of insects and acarines.

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SPECIFICATION

Ethylen Derivatives

This invention relates to new ethylene derivatives, to processes for their preparation, to compositions containing them, to their use as pharmaceuticals, and to their use in the control of insects and acarines.

The new ethylene derivatives of the present invention are those compounds of the formula:—



[wherein R¹ represents a hydroxymethyl or carboxy group, A¹ represents a straight-chain alkylene group containing from 4 to 8 carbon atoms, Y¹ represents a carbonyl or hydroxymethylene group, A² represents a straight- or branched-chain alkylene group containing from 1 to 5 carbon atoms, and R² represents a phenyl, phenoxy or phenylthio group which may carry one or more substituents selected from halogen (e.g. bromine, chlorine or iodine) atoms, straight- or branched-chain alkyl or alkoxy groups, each containing from 1 to 4 carbon atoms, and the trifluoromethyl group] and, when R¹ represents a carboxy group, salts thereof.

In formula I the depicted double bond is in the *trans*-configuration.

As will be appreciated by those skilled in the art, the structure shown in formula I has at least one centre of chirality when Y¹ represents a hydroxymethylene group. Centres of chirality may also occur in compounds of formula I in the groups A² and R². The presence of centres of chirality, as is well known, leads to the existence of isomerism. The present invention includes all such isomers and mixtures thereof.

Classes of preferred compounds of formula I are

- (a) those wherein R¹ represents a hydroxymethyl group;
 - (b) those wherein A¹ represents a straight-chain alkylene group containing 5, 6 or 7, preferably 5, carbon atoms;
 - (c) those wherein Y¹ represents a hydroxymethylene group;
 - (d) those wherein A² represents a straight-chain alkylene group containing 1 or 2, preferably 2, carbon atoms; and
 - (e) those wherein R² represents a phenyl or phenoxy group which may be optionally substituted by a halogen (preferably chlorine) atom or the trifluoromethyl group;
- and especially those such compounds wherein the meanings of symbols R¹, A¹, Y¹, A² and R² are in combination as just stated.

Compounds of formula I of particular importance are

- 10-hydroxy-1-phenoxydec-3-*trans*-en-2-one; AA
- 12-hydroxy-1-phenyldodec-5-*trans*-en-4-one; AB
- 13-hydroxy-1-phenoxytridec-3-*trans*-en-2-one; AC 35
- 11-hydroxy-1-phenylundec-4-*trans*-en-3-one; AD
- 10-hydroxy-1-phenyldec-3-*trans*-en-2-one; AE
- 1-(3-trifluoromethylphenyl)-11-hydroxyundec-4-*trans*-en-3-one; AF
- 1-(4-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one; AG
- 1-(3-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one; AH 40
- 1-(2-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one; AI
- 14-hydroxy-1-phenyltetradec-4-*trans*-en-3-one; AJ
- 11-oxo-12-phenoxydodec-9-*trans*-enoic acid; AK
- (±)-11-phenylundec-7-*trans*-ene-1,9-diol; AL
- (±)-11-(3-trifluoromethylphenyl)undec-7-*trans*-ene-1,9-diol; AM 45
- (±)-10-phenyldec-7-*trans*-ene-1,9-diol; AN
- (±)-12-phenyldodec-7-*trans*-ene-1,9-diol; AO
- (±)-11-(4-chlorophenyl)undec-7-*trans*-ene-1,9-diol; AP
- (±)-11-(3-chlorophenyl)undec-7-*trans*-ene-1,9-diol; AQ
- (±)-11-(2-chlorophenyl)undec-7-*trans*-ene-1,9-diol; AR 50
- 9-oxo-11-phenylundec-7-*trans*-enoic acid; AS
- 9-oxo-10-phenoxydec-7-*trans*-enoic acid; AT
- 9-oxo-10-phenyldec-7-*trans*-enoic acid; AU
- 11-(3-trifluoromethylphenyl)-9-oxoundec-7-*trans*-enoic acid; AV
- 11-(4-chlorophenyl)-9-oxoundec-7-*trans*-enoic acid; AW 55
- 11-(3-chlorophenyl)-9-oxoundec-7-*trans*-enoic acid; AX
- 9-oxo-12-phenyldodec-7-*trans*-enoic acid; AY
- 11-(2-chlorophenyl)-9-oxoundec-7-*trans*-enoic acid; AZ
- (±)-9-hydroxy-11-phenylundec-7-*trans*-enoic acid; BA
- (±)-9-hydroxy-10-phenoxydec-7-*trans*-enoic acid; BB 60
- (±)-11-hydroxy-12-phenoxydodec-9-*trans*-enoic acid; BC

(±)-11-(3-trifluoromethylphenyl)-9-hydroxyundec-7-*trans*-enoic acid;

BD

(±)-9-hydroxy-10-phenyldec-7-*trans*-enoic acid;

BE

(±)-11-(4-chlorophenyl)-9-hydroxyundec-7-*trans*-enoic acid;

BF

(±)-9-hydroxy-12-phenyldodec-7-*trans*-enoic acid;

BG

5 and

(±)-11-(3-chlorophenyl)-9-hydroxyundec-7-*trans*-enoic acid.

BH

5

The letters AA to BH are assigned to the compounds for easy reference later in the specification, for example in the following Tables.

Compounds of outstanding interest are those identified above by the letters AA, AE, AJ, AL, AN,

10 AT, BA and BC.

The compounds of formula I have utility in several areas, for example they are of use in the field of mammalian reproduction, and they are of use in the control of insects and acarines.

10

The utility of the compounds of formula I has been demonstrated in, for example, the following laboratory tests:—

15 T.1. Antifertility in hamsters

15

On the 4th or 5th day of pregnancy, hamsters were each injected subcutaneously with an aqueous solution of a compound of formula I (prepared by dissolving the compound in a minimum volume of ethanol and diluting to the appropriate volume with 0.9% w/v saline). On the 7th day of pregnancy the hamsters were killed and their uteri were examined. Alternatively, the hamsters were dosed on 3 consecutive days (the 3rd, 4th and 5th days of pregnancy) and killed on the 12th day of pregnancy.

20

The dose required for termination of pregnancy in 50% of the hamsters (ED₅₀) was then calculated mathematically.

20

In compounds of the invention, ED₅₀ figures were obtained from, for example, below 0.2 to over 4 mg/kg animal body weight, for example as shown in Table I below.

TABLE I

Compound	Day of Examination	ED ₅₀ (mg/kg)
AA	12	0.4
AD	12	2.0
AE	12	less than 0.5
AJ	12	much less than 0.5
AK	7	3.3
AL	12	0.17
AN	12	0.35
AS	12	1.7
AT	12	0.5
AV	7	4.0
BA	12	0.15
BB	12	2.0
BC	12	0.5

T.2. Stimulation of uterine contraction in rats

Pregnant anaesthetised rats were treated intravenously with the compounds of the invention and the activity of each compound in stimulating uterine contraction was compared with that of a standard compound, the expensive prostaglandin E₁ (PGE₁), and expressed as a ratio.

30

Compounds of the invention were found to be up to at least 0.2 times as active as PGE₁, for example as shown in Table II below.

30

TABLE II

Compound	Activity (compared with PGE ₁)
AC	0.25
AK	0.21
AL	0.28
BC	0.31

T.3. Houseflies

Adult houseflies (*Musca domestica* L.) of mixed sex were injected in the dorsal thorax with 1.0 μ l of a solution of test compound in a mixture of acetone and physiological saline (1:1 v/v). Anaesthesia with carbon dioxide was used, and subsequent holding was at 25°C. A source of honey-water was provided. Fly mortality and oviposition were recorded after 24 hours and egg hatching after 48 hours.

Similar, control, experiments were carried out using a mixture of acetone and physiological saline alone.

The results obtained are shown in Table III below.

TABLE III

Compound	dose (μ g/fly)	% mortality	% egg hatch
AG	0.5	70	100
AH	0.5	90	no eggs
	0.5	40	0
	0.25	30	100
AI	0.5	40	no eggs
	0.5	20	100
	0.25	20	100
AP	0.5	40	no eggs
AW	0.5	60	no eggs
AX	0.5	60	100
AY	0.5	40	50
BF	0.5	50	100
control	0	20	50
	0	10	100
	0	20	100
	0	10	100

T.4. Ticks

First instar ticks (*Ornithodoros moubata* Murray) were allowed to engorge through a stretched artificial membrane (Parafilm M) on blood at 37°C and containing a test compound added in a suitable solvent at a rate of 5.0 μ l per 0.3 ml blood. Mortality and moulting were observed after 14 days holding at 30°C.

The results are shown in Table IV below.

TABLE IV

Compound	% mortality	% moulting normally
AG	0	22
AH	0	10
AI	0	14
AP	0	83
AW	0	0
AX	6	25
AY	22	11
BF	0	13
control	0	25
	0	41

T.5. Mosquitoes

Mosquito larvae (*Aedes aegypti* L.), at the late third or early fourth instar stage, were introduced into water containing a small concentration of a test compound, at 25°C. The water also contained 0.4% v/v acetone, employed as the vehicle for the introduction of the test compound. The larvae were fed with dried powdered bovine liver after 2 hours. After 24 hours at 25°C a mortality count was made, and subsequent metamorphosis and emergence as adults were observed after seven days at 25°C, and compared with controls.

Effective control of the mosquitoes was achieved by, for example, concentrations of test compound of 0.001 to 0.1 parts per million w/v. For example, the minimum effective concentration of compound AI was less than 0.01 parts per million w/v.

Compounds of formula I may be prepared by the application or adaptation of known methods.

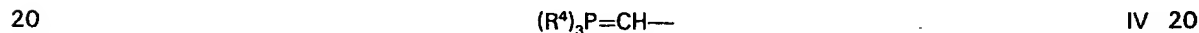
According to a feature of the present invention, compounds of formula I wherein Y¹, represents a carbonyl group, A¹, A², R¹ and R² being as hereinbefore defined, are prepared by the reaction of compound of the formula:—



(wherein A¹ and R¹ are as hereinbefore defined) with compounds of the formula:—



wherein A² and R² are as hereinbefore defined and R³ represents a group of the formula IV or V:—



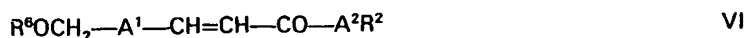
wherein R⁴ represents an alkyl group or a phenyl group unsubstituted or substituted by an alkyl group, and advantageously represents a phenyl or n-butyl group, and R⁵ represents an alkyl group containing from 1 to 4 carbon atoms, preferably a methyl group.

The reaction between compounds of formula II and compounds of formula III wherein R³ represents a group of formula IV (A¹, A², R¹, R² and R⁴ being as hereinbefore defined) is preferably carried out in the presence of an inert organic solvent and preferably at a temperature between 20° and 100°C, for example in the presence of tetrahydrofuran as solvent at the reflux temperature of the reaction mixture or in the presence of hexamethylphosphotriamide as solvent at between 95° and 100°C, optionally under an inert atmosphere (e.g. nitrogen).

The reaction between compounds of formula II and compounds of formula III wherein R³ represents a group of formula V (A¹, A², R¹, R² and R⁵ being as hereinbefore defined) is preferably carried out in the presence of a strong base, for example sodium hydride, preferably in the presence of an inert organic solvent, for example an ether (e.g. tetrahydrofuran), preferably at or near room temperature, e.g. between 10° and 50°C, and optionally under an inert atmosphere (e.g. nitrogen).

According to a further feature of the present invention, compounds of formula I wherein R¹

represents a hydroxymethyl group and Y¹ represents a carbonyl group, A¹, A² and R² being as hereinbefore defined, are prepared from compounds of the formula:—



(wherein A¹, A² and R² are as hereinbefore described and R⁶ represents a protecting group, such as a tetrahydropyran-2-yl group) by the application or adaptation of known methods.

For example, when R⁶ represents a tetrahydropyran-2-yl group the compounds of formula VI may be converted to compounds of formula I by acid hydrolysis. Generally the hydrolysis is carried out in mild conditions, for example using a weak acid such as acetic acid and at or near the ambient temperature.

Compounds of formula VI are generally prepared *in situ*, by the reaction of compounds of the formula:—



(wherein A¹ and R⁶ are as hereinbefore defined) with compounds of formula III (the various symbols being as hereinbefore defined) in conditions similar to those hereinbefore described for the reaction of compounds of formula II with compounds of formula III.

According to a further feature of the present invention, compounds of formula I wherein R¹ represents a carboxy group and Y¹ represents a carbonyl group, A¹, A² and R² being as hereinbefore defined, are prepared by the oxidation of compounds of formula I wherein R¹ represents a hydroxymethyl group and Y¹ represents a carbonyl group or a hydroxymethylene group, A¹, A² and R² being as hereinbefore defined.

The oxidation is carried out in conditions capable of oxidising hydroxymethyl groups to carboxy groups, and of oxidising hydroxymethylene groups (when present) to carbonyl groups, without affecting the rest of the molecule. For example, the oxidation may be carried out by means of chromium trioxide and sulphuric acid in the presence of a suitable organic solvent, for example dimethylformamide, at a temperature near or below the ambient temperature, for example at between -5° and +25°C, preferably in anhydrous conditions.

According to a further feature of the present invention, compounds of formula I wherein Y¹ represents a hydroxymethylene group, A¹, A², R¹ and R² being as hereinbefore defined, are prepared by the reduction of corresponding compounds of formula I wherein Y¹ represents a carbonyl group, using means and conditions capable of reducing carbonyl groups to hydroxymethylene groups without affecting the carbon-carbon double bonds.

The reduction may be effected by a metal borohydride (e.g. sodium borohydride or potassium borohydride), usually in an aqueous, alcoholic or aqueous alcoholic medium and at a temperature between -40° and +30°C, preferably between -5° and +10°C, optionally in the presence of a base, for example an alkali metal hydroxide (e.g. aqueous sodium hydroxide or aqueous potassium hydroxide), or especially when potassium borohydride is employed, in aqueous or aqueous alcoholic conditions buffered at a pH of from pH 7 to pH 9, e.g. at pH 8 (e.g. by the addition of aqueous citric acid solution).

Preferably, the reduction is carried out by means of lithium tri-*s*-butylborohydride in an inert organic solvent (e.g. tetrahydrofuran) preferably at a temperature between -80° and -50°C, and followed by treatment of the reaction mixture with aqueous alkali (e.g. aqueous sodium hydroxide solution) and aqueous hydrogen peroxide solution.

Compounds of formula III may be prepared by the application or adaptation of known methods.

For example, compounds of formula III wherein R³ represents a group of formula IV, A², R² and R⁴ being as hereinbefore defined, may be prepared by the reaction between compounds of the formula:—



(wherein A² and R² are as hereinbefore defined and Q represents a bromine or chlorine atom) and an appropriate trialkyl- or triphenylphosphine in a suitable organic solvent (e.g. chloroform), optionally under a nitrogen atmosphere, preferably under anhydrous conditions and at a temperature of from 20° to 100°C, and advantageously at the reflux temperature of the reaction mixture, followed by reaction of the resulting 2-oxoalkylphosphonium halide of the formula:—



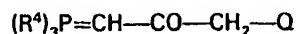
(wherein A², R², R⁴ and Q are as hereinbefore defined) with a base (e.g. aqueous sodium carbonate or ethanolic sodium ethoxide) at ambient temperature.

Alternatively, compounds of formula III wherein R³ represents a group of formula IV, A² represents a methylene group and R² represents an optionally substituted phenoxy or phenylthio group, R⁴ being as hereinbefore defined, may be prepared by the reaction of phenols or thiophenols of the formula:—



X

(wherein R^7X^1 represents an optionally substituted phenoxy or phenylthio group within the definition of R^2 , X^1 representing an oxygen or sulphur atom) with compounds of the formula:—

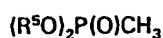


XI

- 5 (wherein R^4 and Q are as hereinbefore defined) in the presence of a base (e.g. potassium hydroxide or sodium ethoxide) and in a suitable solvent (e.g. ethanol), preferably at the reflux temperature of the reaction mixture. 5

- As a further alternative, compounds of formula III wherein R^3 represents a group of formula IV, A^2 , R^2 and R^4 being as hereinbefore defined, may be prepared by the application or adaptation of methods 10 described by Cooke, J. Org. Chem., (1973), 38, 4082. 10

Compounds of formula III wherein R^3 represents a group of formula V, A^2 , R^2 and R^5 being as hereinbefore defined, may be prepared by the treatment of a compound of the formula:—



XII

- 15 (wherein R^5 is as hereinbefore defined) with butyl lithium at a low temperature, e.g. between -45° and $-60^\circ C$, and in an inert organic solvent, e.g. a mixture of tetrahydrofuran and hexane, preferably under an inert atmosphere (e.g. nitrogen) and in anhydrous conditions, followed by treatment of the resulting mixture, containing a compound of the formula:— 15



XII

(wherein R^5 is as hereinbefore defined), with a compound of the formula:—

- 20 $R^8OOC-A^2R^2$ XIV 20

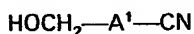
(wherein A^2 and R^2 are as hereinbefore defined and R^8 represents an alkyl, preferably ethyl, group) at a temperature initially between -70° and $-55^\circ C$ and subsequently rising to room temperature.

Compounds of formula VII may be prepared by the application or adaptation of known methods, for example by reduction of compounds of the formula:—

- 25 $R^6OCH_2-A^1-CN$ XV 25

(wherein A^1 and R^6 are as hereinbefore defined), for example by means of diisobutyl aluminium hydride.

Compounds of formula XV may be prepared from compounds of the formula:—



XVI

- 30 (wherein A^1 is as hereinbefore defined) by the application or adaptation of known methods for the protection of hydroxy groups. For example, when R^6 represents a tetrahydropyran-2-yl group, the reaction can be carried out by treatment with dihydropyran, preferably in the presence of a strong acid catalyst, e.g. hydrochloric acid. 30

The salts of the compounds of formula I wherein R^1 represents a carboxy group include pharmaceutically-acceptable salts and agriculturally-acceptable salts.

- 35 By the term "pharmaceutically-acceptable salts", as used in this specification, is meant salts the cations of which are relatively innocuous to the animal organism when used in therapeutic doses so that the beneficial pharmacological properties of the parent carboxylic acid compound of formula I are not vitiated by side-effects ascribable to those cations. 35

- Similarly, by the term "agriculturally acceptable salts", as used in this specification, is meant salts 40 the cations of which are relatively innocuous to the growing or harvested crop. 40

Preferably the salts are water soluble.

Suitable salts include the alkali metal, e.g. sodium and potassium, and ammonium salts and pharmaceutically or agriculturally acceptable amine salts.

- The salts may be prepared from the parent acid compounds of formula I by known methods, for 45 example by reaction of compounds of formula I (wherein R^1 represents a carboxy group) and the appropriate base, e.g. an alkali metal hydroxide or carbonate, ammonium hydroxide, ammonia or an amine, in a suitable solvent which is preferably water in the case of the preparation of alkali metal salts and water or isopropanol in the case of amine salts. The salts may be isolated by lyophilisation of the solution or, if sufficiently insoluble in the reaction medium, by filtration, if necessary after removal of 50 part of the solvent. 50

As well as being useful in themselves as active compounds, salts of the compounds of formula I wherein R¹ represents a carboxy group are useful for the purposes of purification of the parent acids of formula I, for example by exploitation of the solubility differences between the salts and the parent acids in water and in organic solvents, by techniques well known to those skilled in the art. The parent acids of formula I can be regenerated from their salts by known methods, for example by treatment with a mineral acid, e.g. dilute hydrochloric acid.

It is to be understood that, where in this specification reference is made to compounds of formula I, it is intended to refer also, where the context so permits, to the said salts of the compounds of formula I wherein R¹ represents a carboxy group.

As will be readily appreciated by those skilled in the art, the isomeric forms of the compounds of the invention arising from the aforementioned centres of chirality may be separated by the application or adaptation of known methods, for example diastereoisomeric forms may be separated by chromatography using selective adsorption from solution or from the vapour phase onto suitable adsorbents.

By the term "known methods" as used in this specification is meant methods heretofore used or described in the literature.

The following Examples illustrate the preparation of the new ethylene derivatives of the present invention, and the Reference Examples thereafter illustrate the preparation of intermediates.

EXAMPLE 1.

20 Compounds AA and AB

A mixture of 7-hydroxyheptanal (1.3 g) and 2-oxo-3-phenoxypropylenetriphenylphosphorane (4.1 g) in hexamethylphosphotriamide (40 ml) was heated on the steam bath under dry nitrogen for 3 days and was then poured into water (100 ml) and extracted with diethyl ether. The ethereal solution was washed with water, dried over magnesium sulphate, and concentrated to low volume, whereupon triphenylphosphine oxide began to separate. The temperature of the mixture was maintained at 0°C overnight. The mixture was then filtered and the filtrate was concentrated to dryness, to give a mixture (3.7 g) of crude product and triphenylphosphine oxide. A portion (0.4 g) of this residue was purified by preparative thin layer chromatography on silica gel, using a mixture of ethyl acetate, cyclohexane and 90% w/w formic acid (200:200:5 by volume) as eluant, to give 10-hydroxy-1-phenoxydec-3-*trans*-en-2-one (26 mg) in the form of a yellow oil [elemental analysis: C, 71.8; H, 8.1%. C₁₆H₂₂O₃·0.25H₂O requires C, 72.0; H, 8.5%. *r*_{max} 995, 1498, 1600, 1630 and 3350 cm⁻¹. NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 6.25—7.85δ, 2.1—2.5δ, 1.2—2.1δ, triplet at 3.7δ (J=5.5 cycles/second), singlet at 4.73δ].

By proceeding in a similar manner but replacing the 2-oxo-3-phenoxypropylenetriphenylphosphorane, used as starting material, by the appropriate quantity of 4-phenylbutyrylmethylenetriphenylphosphorane, there was prepared 12-hydroxy-1-phenyldodec-5-*trans*-en-4-one [elemental analysis C, 78.9; H, 9.6%. C₁₈H₂₆O₂ requires C, 78.8; H, 9.55%. *r*_{max} 990, 1498, 1630 and 3400 cm⁻¹. NMR (approximately 10% w/v solution in deuteriochloroform): multiplet at 1.1—2.8δ, doublet of triplets at 6.8δ (J=16.5 and 6 cycles/second), triplet at 3.6δ (J=6 cycles/second), doublet at 6.1δ (J=16.5 cycles/second), singlet at 7.25δ].

EXAMPLE 2.

Compound AC

A mixture of 9-(tetrahydropyran-2-yloxy)nonanal (1.0 g) and 2-oxo-3-phenoxypropylenetriphenylphosphorane (1.6 g) in hexamethylphosphotriamide (25 ml) was heated on the steam bath under dry nitrogen for 3 days, and was then poured into water (100 ml) and extracted with diethyl ether. The ethereal extract was washed with water, dried over magnesium sulphate and concentrated to low volume, whereupon triphenylphosphine oxide separated out. This was removed by filtration, and the filtrate was concentrated to dryness. The residue was treated with a mixture of acetic acid (15 ml) and water (7.5 ml), stirred at room temperature for 6 hours, and then evaporated *in vacuo* at a temperature below 50°C. The resulting residue was dissolved in diethyl ether and the ethereal solution was washed with water, with aqueous sodium bicarbonate solution (10% w/v), and with water, dried over magnesium sulphate, and evaporated to leave a residue (1.5 g). A portion (0.3 g) of this residue was purified by preparative thin layer chromatography on silica gel, using a mixture of ethyl acetate, cyclohexane and 90% w/w formic acid (200:200:5 by volume) as eluant, to give 13-hydroxy-1-phenoxytridec-3-*trans*-en-2-one (24 mg) in the form of a yellow oil, which solidified on storage to form a wax, m.p. approximately 32°—35°C. [elemental analysis: C, 74.2; H, 9.15%. C₁₉H₂₈O₃·0.1H₂O requires C, 74.5; H, 9.3%. *r*_{max} 980, 1490, 1595, 1620, 3380 cm⁻¹. NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 6.3—7.6δ, 2.0—2.5δ and 1.2—2.0δ, triplet at 3.6δ (J=6.5 cycles/second), singlet at 4.8δ].

60 EXAMPLE 3.

Compounds AD, AE, AF, AG, AH and AI

A solution of dimethyl 2-oxo-4-phenylbutylphosphate (2.56 g) in anhydrous tetrahydrofuran (50

ml) was added to a stirred suspension of sodium hydride (0.24 g) in anhydrous tetrahydrofuran (20 ml) in an atmosphere of dry nitrogen. The mixture was stirred at ambient temperature for 19 hours and was then treated with a solution of 7-hydroxyheptanal (1.3 g) in hexamethylphosphotriamide (15 ml). The mixture was stirred for a further 5 hours. The solution was then adjusted to pH 4 by the addition of glacial acetic acid and the tetrahydrofuran was removed under reduced pressure. The residue was diluted with diethyl ether and the ethereal solution was washed with water, with saturated aqueous sodium bicarbonate solution, and with water, dried over magnesium sulphate, and evaporated to leave a residue (2.7 g). A portion (0.2 g) of the residue was purified by preparative thin layer chromatography on silica gel, using a mixture of ethyl acetate, cyclohexane and 90% w/w formic acid (200:200:5 by volume) as eluant, to give 11-hydroxy-1-phenylundec-4-*trans*-en-3-one (63 mg) in the form of a pale yellow oil [elemental analysis: C, 78.4; H, 9.2%. $C_{17}H_{24}O$ requires C, 78.4; H, 9.3%. r_{\max} 985, 1628 and 3400 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 6.4—7.1 δ , 1.9—2.4 δ and 1.2—1.9 δ , triplet at 3.6 δ ($J=6$ cycles/second), doublet at 6.05 δ ($J=16$ cycles/second), singlets at 7.2 δ and 2.9 δ].

By proceeding in a similar manner but replacing the dimethyl 2-oxo-4-phenylbutylphosphonate, used as starting material, by the appropriate quantities of dimethyl 2-oxo-3-phenylpropylphosphonate, dimethyl 4-(3-trifluoromethylphenyl)-2-oxobutylphosphonate, dimethyl 4-(4-chlorophenyl)-2-oxobutylphosphonate, dimethyl 4-(3-chlorophenyl)-2-oxobutylphosphonate and dimethyl 4-(2-chlorophenyl)-2-oxobutylphosphonate, respectively, there were prepared

10-hydroxy-1-phenyldec-3-*trans*-en-2-one [elemental analysis: C, 77.0; H, 8.7%. $C_{16}H_{22}O_2 \cdot 0.2H_2O$ requires C, 76.9; H, 9.0%. r_{\max} 980, 1620 and 3400 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 6.65—7.5 δ , 1.0—2.5 δ , triplet at 3.6 δ ($J=6$ cycles/second), doublet at 6.1 δ ($J=16$ cycles/second), singlet at 3.8 δ]. 1-(3-trifluoromethylphenyl)-11-hydroxyundec-4-*trans*-en-3-one [elemental analysis: C, 65.8; H, 7.2%. $C_{18}H_{23}F_3O_2$ requires C, 65.8; H, 7.1%. r_{\max} 985, 1130, 1170, 1625 and 3400 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 7.2—7.6 δ , 6.6—7.1 δ , 2.7—3.2 δ and 1.0—2.5 δ , triplet at 3.6 δ ($J=6$ cycles/second) and doublet at 6.1 δ ($J=16$ cycles/second);

1-(4-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one [elemental analysis: C, 68.9; H, 7.9%; $C_{17}H_{23}ClO_2$ requires C, 69.25; H, 7.9%. r_{\max} 990, 1630 and 3430 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 7.15—7.4 δ , 6.58—7.12 δ , 1.95—2.5 δ and 1.1—1.85 δ , triplet at 3.6 δ ($J=6.5$ cycles/second), doublet at 6.1 δ ($J=15.5$ cycles/second), singlet at 2.9 δ].

1-(3-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one [elemental analysis: C, 69.0; H, 7.8%. $C_{17}H_{23}ClO_2$ requires C, 69.25; H, 7.9%. r_{\max} 985, 1635 and 3450 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 7.0—7.35 δ , 2.8—2.95 δ and 1.1—2.5 δ , doublet of triplets at 6.85 δ ($J=16$ cycles/second and 6.5 cycles/second), triplet at 3.6 δ ($J=6$ cycles/second) and doublet at 6.05 δ ($J=16$ cycles/second)]; and

1-(2-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one [elemental analysis: C, 69.4; H, 8.0%. $C_{17}H_{23}ClO_2$ requires C, 69.25; H, 7.9%. r_{\max} 755, 985, 1630 and 3400 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 6.95—7.5 δ , 2.6—3.3 δ , 1.1—2.6 δ , doublet of triplets at 6.9 δ ($J=16$ cycles/second and 7 cycles/second), triplet at 3.65 δ ($J=6$ cycles/second), doublet at 6.1 δ ($J=16$ cycles/second)].

EXAMPLE 4.

Compound AJ

A solution of dimethyl 2-oxo-4-phenylbutylphosphonate (0.98 g) in anhydrous tetrahydrofuran (15 ml) was added to a stirred suspension of sodium hydride (0.091 g) in anhydrous tetrahydrofuran (20 ml) in an atmosphere of nitrogen. The mixture was stirred at ambient temperature for 24 hours and was then treated with a solution of 9-(tetrahydropyran-2-yloxy)nonanal (0.98 g) in anhydrous tetrahydrofuran (15 ml). The mixture was stirred for a further period of 3 hours. The solution was then adjusted to pH 4 by treatment with acetic acid, the solvent was removed under reduced pressure and the residue was extracted with diethyl ether. The ethereal solution was washed with water, with saturated aqueous sodium bicarbonate solution, and with water, dried over magnesium sulphate, and evaporated. The residue was stirred at ambient temperature with acetic acid (15 ml) and water (7.5 ml) for 7 hours and the mixture was then evaporated *in vacuo* at below 50°C. The residue was dissolved in diethyl ether and the ethereal solution was washed with water, with saturated aqueous sodium bicarbonate solution, and with water, dried over magnesium sulphate, and evaporated to give a residue (1.5 g). A portion (0.3 g) of this residue was purified by preparative thin layer chromatography on silica gel, using a mixture of ethyl acetate, cyclohexane and 90% w/w formic acid (200:200:5 by volume) as eluant, to give 14-hydroxy-1-phenyltetradec-4-*trans*-en-3-one (25 mg) in the form of a yellow oil. [elemental analysis: C, 77.1; H, 10.1%. $C_{20}H_{30}O_2 \cdot 0.5H_2O$ requires C, 77.1; H, 10.0%. r_{\max} 975, 1600, 1630 and 3400 cm^{-1} . NMR (approximately 10% w/v in deutochloroform): multiplets at 6.6—7.2 δ and 1.2—2.5 δ , triplet at 3.65 δ ($J=6$ cycles/second), doublet at 6.1 δ ($J=15.5$ cycles/second), singlets at 7.25 δ and 2.9 δ].

EXAMPLE 5.

Compound AK

A mixture of 8-formyloctanoic acid (1.0 g) and 2-oxo-3-phenoxypropylidene-triphenylphosphorane (2.36 g) in anhydrous hexamethylphosphotriamide (30 ml) was heated on the steam bath under dry nitrogen for 70 hours and was then poured into water (100 ml) and extracted with diethyl ether. The ethereal solution was washed with water and then extracted with aqueous sodium carbonate solution (2N). This aqueous solution was acidified to pH 1 by treatment with dilute hydrochloric acid (2N), and was then saturated with sodium chloride and extracted with diethyl ether. The resulting ethereal solution was washed with water, dried over magnesium sulphate and evaporated to give a residue (1.5 g). A portion (0.3 g) of the residue was purified by preparative thin layer chromatography on silica gel, using a mixture of ethyl acetate, cyclohexane, and 90% w/w formic acid (200:200:5 by volume) as eluant, to give 11-oxo-12-phenoxydodec-9-*trans*-enoic acid (50 mg) in the form of a yellow oil. [elemental analysis: C, 70.3; H, 7.7%. $C_{18}H_{24}O_4 \cdot 0.15H_2O$ requires C, 70.4; H, 8.0%. ν_{\max} 985, 1490, 1625 and 1705 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 6.7—7.6 δ , 2.0—2.6 δ and 1.15—2.0 δ , doublet at 6.4 δ ($J=16$ cycles/second), broad singlet at 9.3 δ , singlet at 4.7 δ].

EXAMPLE 6.

Compounds AL, AM, AN, AO, AP, AQ and AR

A solution of 11-hydroxy-1-phenylundec-4-*trans*-en-3-one (0.5 g) in anhydrous tetrahydrofuran (5 ml) was added dropwise to a stirred solution of lithium tri-*n*-butylborohydride (0.365 g) in anhydrous tetrahydrofuran (1.92 ml) at $-78^\circ C$ under dry nitrogen, and the solution was stirred at $-78^\circ C$ for a further 30 minutes and then at ambient temperature for 3 hours. The stirred mixture was hydrolysed and oxidised by the dropwise addition of aqueous sodium hydroxide solution (3N; 1.4 ml) and aqueous hydrogen peroxide solution (100 volume; 0.88 ml), cooling in an ice bath, and then it was stirred at ambient temperature for one hour. The mixture was then diluted with diethyl ether and water and the resulting organic layer was separated and washed with water, with dilute hydrochloric acid (2N), and with water, then dried over magnesium sulphate and evaporated. The residue was purified by preparative thin layer chromatography on silica gel, using a mixture of ethyl acetate, cyclohexane and 90% w/w formic acid (200:200:5 by volume) as eluant, to give (\pm)-11-phenylundec-7-*trans*-ene-1,9-diol (45 mg) in the form of a pale yellow oil. [elemental analysis: C, 77.8; H, 10.1%. $C_{17}H_{26}O_2$ requires C, 77.8; H, 10.0%. ν_{\max} 990, 1600 and 3400 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 5.25—5.95 δ , 3.9—4.25 δ , 2.5—2.9 δ , 1.15—2.3 δ , triplet at 3.62 δ ($J=6.5$ cycles/second)].

By proceeding in a similar manner but replacing the 11-hydroxy-1-phenylundec-4-*trans*-en-3-one, used as starting material, by the appropriate quantities of 1-(3-trifluoromethylphenyl)-11-hydroxyundec-4-*trans*-en-3-one, 10-hydroxy-1-phenyldec-3-*trans*-en-2-one, 12-hydroxy-1-phenyldec-5-*trans*-en-4-one, 1-(4-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one, 1-(3-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one, and 1-(2-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one, respectively, there were prepared

(\pm)-11-(3-trifluoromethylphenyl)undec-7-*trans*-ene-1,9-diol [elemental analysis: C, 65.4; H, 7.7%. $C_{16}H_{25}F_3O_2$ requires C, 65.4; H, 7.6%. ν_{\max} 800, 970, 995, 1130, 1165 and 3350 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 5.2—5.9 δ , 2.55—3.0 δ and 1.2—2.5 δ , doublet of triplets at 4.05 δ ($J=6$ and 6 cycles/second), triplet at 3.6 δ ($J=5.5$ cycles/second), singlet at 7.45 δ];

(\pm)-10-phenyldec-7-*trans*-ene-1,9-diol [elemental analysis: C, 77.0; H, 9.3%. $C_{16}H_{24}O_2$ requires C, 77.4; H, 9.7%. ν_{\max} 970, 990 and 3380 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 5.25—5.95 δ , 1.1—2.3 δ , doublet of triplets at 4.3 δ ($J=4$ and 6.5 cycles/second), triplet at 3.6 δ ($J=6$ cycles/second), doublet at 2.8 δ ($J=6.5$ cycles/second), singlet at 7.3 δ];

(\pm)-12-phenyldec-*trans*-ene-1,9-diol [elemental analysis: C, 78.2; H, 9.9%. $C_{18}H_{28}O_2$ requires C, 78.2; H, 10.2%. ν_{\max} 970, 995 and 3380 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 5.2—5.95 δ , 3.85—4.25 δ , 2.35—2.8 δ and 1.15—2.3 δ , triplet at 3.6 δ ($J=6.5$ cycles/second), singlet at 7.25 δ];

(\pm)-11-(4-chlorophenyl)undec-7-*trans*-ene-1,9-diol [elemental analysis: C, 68.5; H, 8.5%. $C_{17}H_{25}ClO_2$ requires C, 68.8; H, 8.5%. ν_{\max} 975, 1498 and 3380 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 7.0—7.38 δ , 5.2—5.95 δ , 3.8—4.25 δ , 2.48—2.8 δ and 1.1—2.4 δ , triplet at 3.6 δ ($J=6.5$ cycles/second)];

(\pm)-11-(3-chlorophenyl)undec-7-*trans*-ene-1,9-diol [elemental analysis: C, 68.8; H, 8.7%. $C_{17}H_{25}ClO_2$ requires C, 68.8; H, 8.5%. ν_{\max} 975, 1600 and 3360 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 7.05—7.3 δ , 5.1—6.0 δ , 3.8—4.3 δ , 2.45—2.9 δ and 1.1—2.4 δ , triplet at 3.6 δ ($J=6.5$ cycles/second)]; and

(\pm)-11-(2-chlorophenyl)undec-7-*trans*-ene-1,9-diol [elemental analysis: C, 69.2; H, 8.7%. $C_{17}H_{25}ClO_2$ requires C, 68.8; H, 8.5%. ν_{\max} 755, 975, 1480 and 3380 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 7.0—7.5 δ , 5.2—6.0 δ , 3.8—4.3 δ , 2.5—3.0 δ and 1.0—2.5 δ , triplet at 3.6 δ ($J=6$ cycles/second)].

EXAMPLE 7.

Compounds AS, AT, AU, AV, AW, AX, AY, and AZ

- Anhydrous chromium trioxide (3.46 g) was added portionwise to a stirred solution of 11-hydroxy-1-phenylundec-4-*trans*-en-3-one (2.0 g) in anhydrous dimethylformamide (25 ml) at a temperature below 10°C. The mixture was then treated, dropwise, with a solution of concentrated sulphuric acid (1.08 ml) in dimethylformamide (25 ml) and then the mixture was stirred at 0°C for one hour. It was then treated with diethyl ether (100 ml). The organic solution was decanted off, washed with water, and extracted with aqueous sodium carbonate solution (2N). This aqueous extract was acidified to pH 1 by treatment with dilute hydrochloric acid (2N), then saturated with sodium chloride, and extracted with diethyl ether. The ethereal solution was washed with water, dried over magnesium sulphate, and evaporated to give a residue (0.95 g). A portion (0.2 g) of the residue was purified by preparative thin layer chromatography on silica gel, using a mixture of ethyl acetate, cyclohexane and 90% w/w formic acid (200:200:5 by volume) as eluant, to give 9-oxo-11-phenylundec-7-*trans*-enoic acid (62 mg) in the form of a yellow oil. [elemental analysis: C, 73.9; H, 8.1%. $C_{17}H_{22}O_3 \cdot 0.1H_2O$ requires C, 73.9; H, 8.1%. r_{\max} 980, 1630, 1670 and 1725 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 6.5—7.1 δ , 5.9—6.2 δ and 1.2—3.0 δ , broad singlet at 8.3 δ , singlet at 7.15 δ].
- By proceeding in a similar manner but replacing the 11-hydroxy-1-phenylundec-4-*trans*-en-3-one, used as starting material, by the appropriate quantities of 10-hydroxy-1-phenoxydec-3-*trans*-en-2-one, 10-hydroxy-1-phenyldec-3-*trans*-en-2-one, 1-(3-trifluoromethylphenyl)-11-hydroxyundec-4-*trans*-en-3-one, 1-(4-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one, 1-(3-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one, 12-hydroxy-1-phenyldodec-5-*trans*-en-4-one, and 1-(2-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one, respectively, there were prepared 9-oxo-10-phenoxydec-7-*trans*-enoic acid [elemental analysis: C, 68.2; H, 7.3%. $C_{16}H_{20}O_4 \cdot 0.25H_2O$ requires C, 68.4; H, 7.4%. r_{\max} 980, 1500, 1600, 1635 and 1720 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 6.3—7.5 δ , 2.05—2.76 δ and 1.2—2.05 δ , broad singlet at 9.3 δ , singlet at 4.75 δ]; 9-oxo-10-phenyldec-7-*trans*-enoic acid [elemental analysis: C, 72.5; H, 7.6%. $C_{16}H_{20}O_3 \cdot 0.25H_2O$ requires C, 72.6; H, 7.8%. r_{\max} 980, 1495, 1620 and 1715 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 6.6—7.6 δ , 5.7—6.3 δ , 3.6—4.0 δ , 2.0—2.6 δ and 1.1—2.0 δ , singlet at 9.0 δ]; 11-(3-trifluoromethylphenyl)-9-oxoundec-7-*trans*-enoic acid [elemental analysis: C, 63.3; H, 6.3%. $C_{18}H_{21}F_3O_3$ requires C, 63.15; H 6.2%. r_{\max} 800, 980, 1130, 1165, 1630 and 1715 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 7.4—7.55 δ , 2.74—3.4 δ , 2.0—2.74 δ and 0.9—2.0 δ , doublet of triplets at 6.85 δ ($J=6.75$ and 16.25 cycles/second), doublet at 6.1 δ ($J=16.5$ cycles/second), singlet at 10.3 δ]; 11-(4-chlorophenyl)-9-oxoundec-7-*trans*-enoic acid, m.p. 62°—63°C [elemental analysis: C, 65.1; H, 6.8%. $C_{17}H_{21}ClO_3 \cdot 0.25H_2O$ requires C 65.1; H, 6.9%. r_{\max} 985, 1500, 1635 and 1700 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 7.18—7.48 δ , 6.5—7.18 δ , 2.0—2.7 δ and 1.18—2.0 δ , doublet at 6.1 δ ($J=16$ cycles/second), broad singlet at 10.35 δ , singlet at 2.88 δ]; 11-(3-chlorophenyl)-9-oxoundec-7-*trans*-enoic acid [elemental analysis: C, 65.9; H, 6.8%. $C_{17}H_{21}ClO_3$ requires C, 66.1; H, 6.9%. r_{\max} 985, 1485, 1635 and 1700 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 7.05—7.35 δ , 2.7—3.1 δ and 1.15—2.7 δ , doublet of triplets at 6.85 δ ($J=16$ cycles/second and 7 cycles/second), doublet at 6.1 δ ($J=16$ cycles/second), broad singlet at 10.5 δ]; 9-oxo-12-phenyldodec-7-*trans*-enoic acid [elemental analysis: C, 74.5; H, 8.5%. $C_{18}H_{24}O_3 \cdot 0.1H_2O$ requires C, 74.5; H, 8.4%. r_{\max} 985, 1635 and 1715 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 1.1—3.2 δ , doublet of triplets at 6.82 δ ($J=16.5$ cycles/second and 6.5 cycles/second), doublet at 6.08 δ ($J=16.5$ cycles/second), singlets at 10.15 δ and 7.28 δ]; and 11-(2-chlorophenyl)-9-oxoundec-7-*trans*-enoic acid [elemental analysis: C, 65.9; H, 7.2%. $C_{17}H_{21}ClO_3$ requires C, 66.1; H, 6.9%. r_{\max} 755, 985, 1480, 1630 and 1700 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 7.0—7.5 δ , 2.6—3.3 δ and 1.15—2.6 δ , doublet of triplets at 6.87 δ ($J=16$ cycles/second and 6.5 cycles/second), doublet at 6.1 δ ($J=16$ cycles/second), broad singlet at 10.77 δ].

EXAMPLE 8.

Compounds BA, BB, BC, BD, BE, BF, BG and BH

- A solution of 9-oxo-11-phenylundec-7-*trans*-enoic acid (0.75 g) in anhydrous tetrahydrofuran (10 ml) was added to a stirred solution of lithium tri-*s*-butylborohydride (1.04 g) in anhydrous tetrahydrofuran (5.47 ml) at -78°C, under dry nitrogen. The solution was stirred at -78°C for 30 minutes and then at ambient temperature for 3 hours, followed by hydrolysis and oxidation by means of the dropwise addition of aqueous sodium hydroxide solution (3N; 4.03 ml) and aqueous hydrogen peroxide solution (100 volumes; 2.5 ml), cooling in an ice bath. The mixture was stirred for one hour at ambient temperature and then was diluted with water. The aqueous phase was separated, washed with diethyl ether, and then acidified to pH 1 by treatment with hydrochloric acid (2N) and extracted with diethyl ether. The ethereal solution was washed with water, dried over magnesium sulphate and

evaporated to give a residue (0.7 g). A portion (0.3 g) of the residue was purified by preparative thin layer chromatography on silica gel, using a mixture of ethyl acetate, cyclohexane, and 90% w/w formic acid (200:200:5 by volume) as eluant, to give (\pm)-9-hydroxy-11-phenylundec-7-*trans*-enoic acid (35 mg) in the form of a yellow oil. [elemental analysis: C, 73.7; H, 8.8%. $C_{17}H_{24}O_3$ requires C, 73.9; H,

5 8.75%. r_{\max} 970, 990, 1600, 1710 and 3400 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 7.1—7.3 δ , 5.2—6.15 δ , 3.9—4.2 δ , 2.5—2.8 δ and 1.1—2.5 δ]. 5

By proceeding in a similar manner but replacing the 9-oxo-11-phenylundec-7-*trans*-enoic acid, used as starting material, by the appropriate quantities of 9-oxo-10-phenoxydec-7-*trans*-enoic acid, 11-oxo-12-phenoxydodec-9-*trans*-enoic acid, 11-(3-trifluoromethylphenyl)-9-oxoundec-7-*trans*-enoic acid, 9-oxo-10-phenyldec-7-*trans*-enoic acid, 11-(4-chlorophenyl)-9-oxoundec-7-*trans*-enoic acid, 9-oxo-12-phenyldodec-7-*trans*-enoic acid, and 11-(3-chlorophenyl)-9-oxoundec-7-*trans*-enoic acid, respectively, there were prepared

(\pm)-9-hydroxy-10-phenoxydec-7-*trans*-enoic acid [elemental analysis: C, 67.9; H, 7.8%. $C_{18}H_{22}O_4 \cdot 0.25H_2O$ requires C, 67.9; H, 8.0%. r_{\max} 975, 995, 1600, 1710 and 3400 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 6.8—7.5 δ , 5.3—6.2 δ , 4.35—4.7 δ , 3.8—4.1 δ and 1.1—2.6 δ]; 15

(\pm)-11-hydroxy-12-phenoxydodec-9-*trans*-enoic acid [elemental analysis: C, 70.3; H, 8.55%. $C_{18}H_{26}O_4$ requires C, 70.6; H, 8.55%. r_{\max} 970, 990, 1600, 1710 and 3400 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 6.72—7.5 δ , 6.0—6.7 δ , 5.2—5.9 δ , 4.3—4.6 δ , 3.8—3.95 δ , 1.8—2.5 δ and 1.1—1.8 δ]; 20

(\pm)-11-(3-trifluoromethylphenyl)-9-hydroxyundec-7-*trans*-enoic acid [elemental analysis: C, 63.0; H, 7.0%; $C_{18}H_{23}F_3O_3$ requires C, 62.8; H, 6.7%. r_{\max} 805, 975, 1130, 1160, 1720 and 3450 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 5.2—6.0 δ , 3.8—4.3 δ and 1.0—3.2 δ , singlets at 7.4 δ and 6.75 δ]; 25

(\pm)-9-hydroxy-10-phenyldec-7-*trans*-enoic acid [r_{\max} 970, 1710 and 3450 cm^{-1} . m/e 244, 171, 153, 135, 125, 92, 91]; 25

(\pm)-11-(4-chlorophenyl)-9-hydroxyundec-7-*trans*-enoic acid [elemental analysis: C, 65.7; H, 7.4%. $C_{17}H_{23}ClO_3$ requires C, 65.7; H, 7.5%. r_{\max} 978, 1500, 1720 and 3400 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 7.0—7.5 δ , 5.2—5.95 δ , 3.9—4.3 δ and 1.15—2.9 δ , singlet at 6.72 δ]; 30

(\pm)-9-hydroxy-12-phenyldodec-7-*trans*-enoic acid [elemental analysis: C, 73.7; H, 8.9%. $C_{18}H_{26}O_3 \cdot 0.2H_2O$ requires C, 73.5; H, 9.05%. r_{\max} 975, 1500, 1720 and 3400 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 5.2—5.8 δ , 3.9—4.25 δ , and 1.15—2.85 δ , singlets at 7.3 δ and 6.4 δ]; and 35

(\pm)-11-(3-chlorophenyl)-9-hydroxyundec-7-*trans*-enoic acid [elemental analysis: C, 66.0; H, 7.8%. $C_{17}H_{23}ClO_3$ requires C, 65.7; H, 7.5%. r_{\max} 975, 1600, 1715 and 3400 cm^{-1} . NMR (approximately 10% w/v solution in deuteriochloroform): multiplets at 7.0—7.35 δ , 5.2—6.0 δ , 3.85—4.25 δ and 1.0—3.0 δ , singlet at 6.3 δ]. 35

REFERENCE EXAMPLE 1.

40 A solution of diisobutyl aluminium hydride (6.45 g) in anhydrous toluene (20 ml) was added dropwise to a stirred solution of 1-cyano-9-(tetrahydropyran-2-yloxy)-nonane (5.0 g) in anhydrous diethyl ether (60 ml) at 10°—15°C. The resulting solution was stirred at ambient temperature for 90 minutes and then it was added dropwise to dilute acetic acid (2N; 120 ml), in an ice-salt bath, maintaining the temperature below 15°C. The organic phase was separated and the aqueous phase 45 was extracted with diethyl ether, and then the combined organic solutions were washed with water, with saturated aqueous sodium bicarbonate solution, and with water, and then dried over magnesium sulphate. Evaporation of the solution gave an oily residue (4.6 g) which was distilled, to give 9-(tetrahydropyran-2-yloxy)nonanal (1.9 g) in the form of a viscous colourless oil, b.p. 140°—160°C/0.08 mm Hg. (r_{\max} 815, 868, 905, 1035, 1075, 1200, 1725 and 2700 cm^{-1}). 45

50 REFERENCE EXAMPLE 2.

Dihydropyran (12.2 g) was added, dropwise, to a stirred mixture of 9-cyanononanol (12.0 g) and concentrated hydrochloric acid (4 drops), maintaining the temperature below 65°C. After the addition was complete the mixture was stirred at 65°—70°C for 3 hours and then at ambient temperature for 90 minutes and then it was poured into a mixture of ice and water (130 ml) containing aqueous sodium 55 hydroxide solution (2N; 20 ml). The mixture was extracted with diethyl ether and the ethereal solution was washed with water, dried over anhydrous sodium carbonate and evaporated. The residue was distilled (from a trace of anhydrous potassium acetate) to give 1-cyano-9-(tetrahydropyran-2-yloxy)nonane (12.4 g) in the form of a colourless oil, b.p. 150°—155°C/0.1 mm Hg. [elemental analysis: C, 71.3; H, 11.0; N, 5.3%. $C_{15}H_{27}NO_2$ requires C, 71.1; H, 10.7; N, 5.5%. r_{\max} 815, 868, 905, 1035, 1075, 1200, 1350 and 2220 cm^{-1} . NMR (approximately 10% w/v solution in 60 deuteriochloroform): multiplets at 3.15—4.15 δ and 1.18—2.0 δ , triplet at 2.3 δ ($J=6.5$ cycles/second), broad singlet at 4.6 δ]. 60

REFERENCE EXAMPLE 3.

A solution of n-butyl lithium (5.88 g) in hexane (48 ml) and anhydrous diethyl ether (70 ml) was added to a stirred solution of dimethyl methylphosphonate (11.4 g) in anhydrous tetrahydrofuran (50 ml) at -50°C in an atmosphere of nitrogen during 20 minutes. The solution was stirred for a further 15 minutes at -60°C , and was then treated with a solution of ethyl 3-(3-trifluoromethylphenyl)propionate (11.3 g) in anhydrous tetrahydrofuran (20 ml) during 10 minutes at -60°C . The solution was stirred at -60°C for 90 minutes and then at ambient temperature for 2 hours. The solution was then treated with acetic acid (10 ml) and the solvents were evaporated off under reduced pressure. Water (75 ml) was added to the resulting gelatinous residue and the mixture was extracted with diethyl ether. The ethereal solution was washed with water, with aqueous sodium bicarbonate solution (10% w/v), and with water, dried over magnesium sulphate, and evaporated. The residue was distilled to give dimethyl 4-(3-trifluoromethylphenyl)-2-oxobutylphosphonate (7.4 g) in the form of a colourless oil, b.p. $157^{\circ}\text{--}159^{\circ}\text{C}/0.2\text{ mm Hg}$. [elemental analysis: C, 48.3; H, 5.1; P, 9.8%. $\text{C}_{13}\text{H}_{16}\text{F}_3\text{O}_4\text{P}$ requires C, 48.15; H, 5.0; P, 9.55%. r_{max} 1035, 1125, 1165, 1265, 1330, 1555 and 1720 cm^{-1}].

By proceeding in a similar manner but replacing the ethyl 3-(3-trifluoromethylphenyl)propionate, used as a starting material, by the appropriate quantities of ethyl 3-(4-chlorophenyl)propionate, ethyl 3-(3-chlorophenyl)propionate and ethyl 3-(2-chlorophenyl)propionate, respectively, there were prepared dimethyl 4-(4-chlorophenyl)-2-oxobutylphosphonate, b.p. $180^{\circ}\text{--}184^{\circ}\text{C}/0.2\text{ mm Hg}$. [elemental analysis: C, 49.8; H, 5.7; P, 10.5%. $\text{C}_{12}\text{H}_{16}\text{ClO}_4\text{P}$ requires C, 49.6; H, 5.55; P, 10.7%. r_{max} 820, 1040, 1270, 1495 and 1720 cm^{-1}]; dimethyl 4-(3-chlorophenyl)-2-oxobutylphosphonate b.p. $178^{\circ}\text{--}184^{\circ}\text{C}/0.15\text{ mm Hg}$. [elemental analysis: C, 49.2; H, 5.8; P, 10.5%. $\text{C}_{12}\text{H}_{16}\text{ClO}_4\text{P}$ requires C, 49.6; H, 5.55; P, 10.7%. r_{max} 815, 1035, 1265, 1483 and 1720 cm^{-1}]; and dimethyl 4-(2-chlorophenyl)-2-oxobutylphosphonate, b.p. $178^{\circ}\text{--}188^{\circ}\text{C}/0.15\text{ mm Hg}$. [elemental analysis: C, 49.8; H, 5.7; P, 10.8%. $\text{C}_{12}\text{H}_{16}\text{ClO}_4\text{P}$ requires C, 49.6; H, 5.55; P, 10.7%. r_{max} 760, 1040, 1270, 1480 and 1720 cm^{-1}].

REFERENCE EXAMPLE 4.

A solution of 3-(3-trifluoromethylphenyl)propionic acid (13.6 g) in anhydrous ethanol (25 ml) containing concentrated sulphuric acid (1.5 ml) was heated at reflux for 24 hours and was then poured into water (100 ml). The mixture was extracted with diethyl ether and the ethereal extract was washed with water, with aqueous sodium carbonate solution (2N), and with water, then dried over magnesium sulphate and evaporated. The resulting residue was distilled to give ethyl 3-(3-trifluoromethylphenyl)propionate (11.5 g) in the form of a colourless oil, b.p. $133^{\circ}\text{--}135^{\circ}\text{C}/17\text{ mm Hg}$. [elemental analysis: C, 58.6; H, 5.2%. $\text{C}_{12}\text{H}_{13}\text{F}_3\text{O}_2$ requires C, 58.5; H, 5.3%. r_{max} 1125, 1170, 1330 and 1740 cm^{-1}].

The compounds of formula I are useful in modifying, qualitatively or quantitatively, or synchronising various functions of female mammalian reproductive systems.

The compounds of formula I are useful in the control of insects and acarines, for example they are effective against *Hemiptera*, for example *Lygaeidae*, *Miridae* and *Pyrrhocoridae*; against *Lepidoptera*, for example *Pyralidae*, *Noctuidae* and *Gelechiidae*, against *Coleoptera*, for example *Tenebrionidae*, *Chrysomelidae* and *Dermestidae*; against *Diptera*, for example mosquitoes and flies; and *Homoptera*, for example aphids; and other insects and acarines.

The compounds of formula I may be used to control insects and acarines which are injurious to growing crops, stored products including foodstuffs, household goods, timber, property, farm and domestic or other desirable animals, and humans, to control insects and acarines which spread or act as vectors of disease to man, to animals, or to plants, and to control insects which are aesthetically undesirable.

Suitable means of applying the compounds of formula I in the control of insects and acarines include:—

- to growing crops as foliar sprays, dusts, granules and foams; and as suspensions of finely divided and encapsulated compounds of formula I; as soil and root treatments by liquid drenches, dusts, granules, smokes and foams; and as seed dressings by liquid slurries and dusts.
- to stored products, timber and household goods as sprays, dusts and smokes, or incorporated into strips of polymers; as poisoned baits for the control of grasshoppers and locusts and other arthropod pests.
- to persons or animals infested by or exposed to infestation by arthropods or to their immediate vicinity (e.g. housing) as sprays, baths, jets, dips, showers, fogs, dusts, livestock self-treatment systems, greases, wax-smears, creams and shampoos, or to persons or animals infested by or exposed to infestation by arthropods by parenteral or oral administration (e.g. incorporated in feed or suitable pharmaceutical formulations), or to the environment in general or in specific locations where pests may lurk as sprays, fogs, dusts, greases, wax-smears, smokes, lacquers, granules and trickle feeds to waterways.

The present invention includes within its scope pharmaceutical compositions (including veterinary

compositions) which comprise at least one compound of the invention together with a pharmaceutical carrier or coating. In clinical practice the compounds of the present invention will normally be administered orally, rectally, vaginally or parenterally.

5 Solid compositions for oral administration include compressed tablets, pills, dispersible powders, and granules. 5

Liquid compositions for oral administration include pharmaceutically acceptable emulsions, solutions, suspensions, syrups and elixirs.

The compositions according to the invention, for oral administration, also include capsules of absorbable material such as gelatin containing one or more of the compounds of the invention.

10 Solid compositions for vaginal administration include pessaries. 10

Solid compositions for rectal administration include suppositories.

Preparations according to the invention for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, or emulsions.

15 The compounds of the invention may alternatively be administered orally in the form of an aerosol. 15

Methods of presentation of pharmaceutically active compounds are well known in the art and a suitable vehicle may be determined by the physician, pharmacist or veterinarian, depending upon such factors as the effect sought, the size, age, sex and condition of the patient and, for veterinary uses, species of the animal to be treated, and on the physical properties of the active compound. The compositions may also contain, as is usual in the art, such materials as solid or liquid adjuvants, for

20 example wetting agents, preservatives, flavouring and colouring agents. 20

The percentage of active ingredient in the compositions of the invention may be varied, it being necessary that it should constitute a proportion such that a suitable dosage for the therapeutic effect desired shall be obtained. Obviously several unit dosage forms may be administered at about the same time.

25 In general, the compositions for the modification or synchronisation of functions of female mammalian reproductive systems should normally contain at least 0.025% by weight of active substance when required for administration by injection; for oral administration the preparations will normally contain at least 0.1% by weight of active substance. 25

30 The dose employed depends upon the desired therapeutic effect, the route of administration and the duration of the treatment. The doses are generally, for example, between 1 μ g and 50 mg/kg body weight by intravaginal or intracervical administration, between 0.1 μ g and 2.0 mg/kg body weight by intravenous administration, and between 10 μ g and 10 mg/kg body weight orally. 30

If necessary these doses may be repeated as and when required.

The following Example illustrates pharmaceutical compositions according to the invention.

35 EXAMPLE 9. 35

Witepsol S—58 (a pessary-base supplied by Dynamit Nobel A.G.) (2 g) was melted at below 40°C and there was added to it (\pm)-11-phenylundec-7-*trans*-ene-1,9-diol (2 mg). After mixing to form a suspension, the suspension was poured into a pessary mould and cooled until the suspension became solid.

40 According to a further feature of the invention, there are provided compositions suitable for use against insects and acarines, containing as active ingredient at least one of the compounds of formula I in association with one or more diluents compatible with the compounds of formula I. 40

Solid compositions according to the invention suitable for use as aforesaid for application to growing crops or crop-growing loci contain at least one compound of formula I admixed with one or more solid diluents. 45

50 Suitable solid diluents include aluminium silicate, kieselguhr, corn husks, tricalcium phosphate, powdered cork, adsorbent carbon black, magnesium silicate, a clay such as kaolin, bentonite or attapulgite, and water soluble polymers and such solid compositions may, if desired, contain one or more compatible wetting, dispersing, emulsifying or colouring agents which, when solid, may also serve as diluent. 50

55 Such solid compositions may take the form of, for example, dusts, granules or wettable powders. Liquid compositions for application to growing crops and crop-growing loci according to the invention may take the form of solutions, suspensions and emulsions of one or more of the compounds of formula I, optionally encapsulated in natural or synthetic polymers, and may, if desired, incorporate wetting, dispersing or emulsifying agents. 55

Compositions in the form of aerosols containing one or more of the compounds of formula I are also within the scope of the present invention.

If desired, the compositions according to the present invention suitable for use against insects and acarines may contain other adjuvants such as adhesives.

60 The liquid compositions hereinbefore described for application to growing crops and crop-growing loci may, in general, alternatively be employed as trickle feedstocks to treat flowing water. Standing or flowing waters may also be treated with compounds of formula I formulated in homogenous or heterogenous granules, pellets or capsules designed to release their active constituents over a period of time. 60

The compositions hereinbefore described for application to growing crops and crop-growing loci may, in general, alternatively be employed for topical application to man and animals and in the protection of stored products, household goods, property and areas of the general environment.

5 Solid compositions in the form of dusts hereinbefore described for application to growing crops or crop-growing loci may, in general, alternatively be employed contained in bags or sacks in such a manner as to permit self-treatment by cattle. 5

Oily solutions may be applied to backrubbers used by cattle to achieve self-medication by them.

10 Compositions in the form of solutions or suspensions together, if desired, with additives as described above, in vegetable oil or other greases, paraffin wax or other waxes, or lacquers or creams, for application to large or small animals or parts thereof to control or prevent attacks by arthropods are also included in the invention. 10

15 According to a further feature of the invention, there are provided solid or liquid baits suitable for insecticidal and acaricidal use comprising at least one compound of formula I. The bait employed in addition to the carrier or diluent material, which may include a food substance to induce consumption, may include any substance to which the insect or acarine is attracted. 15

Compositions according to the present invention may also contain herbicides, fungicides, other insecticides and acaricides, fertilisers, antiseptic agents, bacteriostats, bactericidal agents, sporicidal agents and auxiliary therapeutic agents, as well as reodorants and colouring agents.

20 The compositions for use against insects and acarines according to the invention usually contain between 0.0001% and 95%, more particularly between 0.0005% and 50%, by weight of at least one of the compounds of formula I. The actual compositions employed and their rate of application shall be those considered necessary to achieve the desired effect(s) by the farmer, livestock producer, medical or veterinary practitioner, pest control operator or other person skilled in the art. Solid and liquid compositions for application to growing crops and crop-growing loci, topically to animals, to timber and 25 to stored products, household goods and their environs usually contain between 0.0005% and 50%, more particularly between 0.01% and 10%, by weight of compounds of formula I. 25

The following Examples illustrate compositions for the control of insects and acarines according to the present invention.

EXAMPLE 10.

30 Granules of the following constitution were prepared by the application of known methods. 30

1-(3-chlorophenyl)-11-hydroxyundec-4-trans-en-3-one 5% w/w

Waxoline Red OS (a red axo dye) 0.2% w/w

30/60 Attaclay granules (sorpitive silica clay) to 100% by weight.

EXAMPLE 11.

35 A water soluble concentrate of the following constitution was prepared by the application of known methods. 35

11-(4-chlorophenyl)-9-oxoundec-7-trans-enoic acid 10% w/v

Ethylan KEO (nonylphenol ethylene oxide condensate) 10% w/v

dimethylformamide to 100% by volume.

40 CLAIMS 40

1. Ethylene derivatives of the formula:—



[wherein R^1 represents a hydroxymethyl or carboxy group, A^1 represents a straight-chain alkylene group containing from 4 to 8 carbon atoms, Y^1 represents a carbonyl or hydroxymethylene group, A^2 45 represents a straight- or branched-chain alkylene group containing from 1 to 5 carbon atoms, and R^2 represents a phenyl, phenoxy or phenylthio group which may carry one or more substituents selected from halogen atoms, straight- or branched-chain alkyl or alkoxy groups, each containing from 1 to 4 carbon atoms, and the trifluoromethyl group] and, when R^1 represents a carboxy group, salts thereof. 45

2. Ethylene derivatives according to claim 1 wherein R^1 represents the hydroxymethyl group.

50 3. Ethylene derivatives according to claim 1 or 2 wherein A^1 represents a straight-chain alkylene group containing 5, 6 or 7 carbon atoms. 50

4. Ethylene derivatives according to claim 1 or 2 wherein A^1 represents the pentamethylene group.

5. Ethylene derivatives according to any one of claims 1 to 4 wherein Y^1 represents the hydroxymethylene group.

15

6. Ethylene derivatives according to any one of claims 1 to 5 wherein A² represents a straight-chain alkylene group containing 1 or 2 carbon atoms.

7. Ethylene derivatives according to any one of claims 1 to 5 wherein A² represents the ethylene group.

5 8. Ethylene derivatives according to any one of claims 1 to 7 wherein R² represents a phenyl or phenoxy group which may be optionally substituted by a halogen atom or the trifluoromethyl group. 5

9. Ethylene derivatives according to claim 8 wherein R² represents a phenyl or phenoxy group substituted by a chlorine atom.

10. 10-Hydroxy-1-phenoxydec-3-*trans*-en-2-one.

10 11. 10-Hydroxy-1-phenyldec-3-*trans*-en-2-one. 10

12. 14-Hydroxy-1-phenyltetradec-4-*trans*-en-3-one.

13. (±)-11-Phenylundec-7-*trans*-ene-1,9-diol.

14. (±)-10-Phenyldec-7-*trans*-ene-1,9-diol.

15. 9-Oxo-10-phenoxydec-7-*trans*-enoic acid and salts thereof.

15 16. (±)-9-Hydroxy-11-phenylundec-7-*trans*-enoic acid and salts thereof. 15

17. (±)-11-Hydroxy-12-phenoxydodec-9-*trans*-enoic acid and salts thereof.

18. An ethylene derivative according to claim 1 selected from 12-hydroxy-1-phenyldodec-5-*trans*-en-4-one, 13-hydroxy-1-phenoxytridec-3-*trans*-en-2-one, 11-hydroxy-1-phenylundec-4-*trans*-en-3-one, 1-(3-trifluoromethylphenyl)-11-hydroxyundec-4-*trans*-en-3-one, 1-(4-chlorophenyl)-11-

20 hydroxyundec-4-*trans*-en-3-one, 1-(3-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one, 1-(2-chlorophenyl)-11-hydroxyundec-4-*trans*-en-3-one, 11-oxo-12-phenoxydodec-9-*trans*-enoic acid, (±)-11-(3-trifluoromethylphenyl)undec-7-*trans*-ene-1,9-diol, (±)-12-phenyldodec-7-*trans*-ene-1,9-diol, (±)-11-(4-chlorophenyl)undec-7-*trans*-ene-1,9-diol, (±)-11-(3-chlorophenyl)undec-7-*trans*-ene-1,9-diol, (±)-11-(2-chlorophenyl)undec-7-*trans*-ene-1,9-diol, 9-oxo-11-phenylundec-7-*trans*-enoic acid, 9-

25 oxo-10-phenyldec-7-*trans*-enoic acid, 11-(3-trifluoromethylphenyl)-9-oxoundec-7-*trans*-enoic acid, 11-(4-chlorophenyl)-9-oxoundec-7-*trans*-enoic acid, 11-(3-chlorophenyl)-9-oxoundec-7-*trans*-enoic acid, 9-oxo-12-phenyldodec-7-*trans*-enoic acid, 11-(2-chlorophenyl)-9-oxoundec-7-*trans*-enoic acid, (±)-9-hydroxy-10-phenoxydec-7-*trans*-enoic acid, (±)-11-(3-trifluoromethylphenyl)-9-hydroxyundec-7-

25 *trans*-enoic acid, (±)-9-hydroxy-10-phenyldec-7-*trans*-enoic acid, (±)-11-(4-chlorophenyl)-9-hydroxyundec-7-*trans*-enoic acid, (±)-9-hydroxy-12-phenyldodec-7-*trans*-enoic acid and (±)-11-(3-chlorophenyl)-9-hydroxyundec-7-*trans*-enoic acid, and salts of any of the aforementioned acids.

30 19. A process for the preparation of an ethylene derivative of the formula depicted in claim 1 wherein Y¹ represents a carbonyl group and A¹, A², R¹ and R² are as defined in claim 1, which comprises the reaction of a compound of the formula:—

35 II
$$R^1-A^1-CHO$$
 35

(wherein A¹ and R¹ are as defined in claim 1) with a compound of the formula:—

III
$$R^3-CO-A^2R^2$$

wherein A² and R² are as defined in claim 1 and R³ represents a group of the formula IV or V:—

$$(R^4)_3P=CH-$$
 IV

40
$$(R^5O)_2P(O)CH_2-$$
 V 40

wherein R⁴ represents an alkyl group or a phenyl group unsubstituted or substituted by an alkyl group, and R⁵ represents an alkyl group containing from 1 to 4 carbon atoms.

20. A process for the preparation of an ethylene derivative of the formula depicted in claim 1 wherein R¹ represents a hydroxymethyl group and Y¹ represents a carbonyl group and A¹, A² and R² are as defined in claim 1, which comprises treating a compound of the formula:— 45

$$R^6OCH_2-A^1-CH=CH-CO-A^2R^2$$
 VI

(wherein A¹, A² and R² are as defined in claim 1 and R⁶ represents a protecting group, such as a tetrahydropyran-2-yl group) by a known method to convert the grouping R⁶OCH₂— to the hydroxymethyl group.

50 21. A process for the preparation of an ethylene derivative of the formula depicted in claim 1 wherein R¹ represents a carboxy group, Y¹ represents a carbonyl group, and A¹, A² and R² are as defined in claim 1, which comprises the oxidation of a compound of the said formula (wherein R¹ represents a hydroxymethyl group, Y¹ represents a carbonyl group or a hydroxymethylene group, and A¹, A² and R² are as defined in claim 1) to convert the hydroxymethyl group R¹, and Y¹ when Y¹ represents the hydroxymethylene group, to a carboxy group or a carbonyl group respectively, without affecting the rest 55 of the molecule.

22. A process for the preparation of an ethylene derivative of the formula depicted in claim 1 wherein Y¹ represents a hydroxymethyl ne group and A¹, A², R¹ and R² are as defined in claim 1, which comprises the reduction of a corresponding compound of the said formula wherein Y¹ represents a carbonyl group, by a known method for reducing a carbonyl group to hydroxymethylene without affecting a carbon-carbon double bond. 5
23. A process according to any one of claims 19, 21 or 22 followed by the step of converting a product obtained of the formula depicted in claim 1 wherein R¹ represents a carboxy group by a known method into a pharmaceutically-acceptable or agriculturally-acceptable salt.
24. A process for the preparation of ethylene derivatives of the formula specified in claim 1 and, when R¹ represents a carboxy group, salts thereof substantially as hereinbefore described with especial reference to any one of Examples 1 to 8. 10
25. Ethylene derivatives of the formula specified in claim 1 and, when appropriate, salts thereof when prepared by a process claimed in any one of claims 19 to 24.
26. Pharmaceutical compositions (including veterinary compositions) which comprise, as active ingredient, at least one ethylene derivative as claimed in any one of claims 1 to 18, or—when appropriate—a pharmaceutically-acceptable salt thereof, in association with a pharmaceutical carrier or coating. 15
27. Pharmaceutical compositions according to claim 26 substantially as hereinbefore described with especial reference to Example 9.
28. The use of an ethylene derivative as claimed in any one of claims 1 to 18, or—when appropriate—a pharmaceutically-acceptable salt thereof, for the modification or synchronisation of female mammalian reproductive systems. 20
29. Compositions suitable for use against insects and acarines which comprise, as active ingredient, at least one ethylene derivative as claimed in any one of claims 1 to 18, or—when appropriate—an agriculturally acceptable salt thereof, in association with one or more diluents compatible with the said compound. 25
30. Compositions according to claim 29 substantially as hereinbefore described with especial reference to Example 10 or 11.
31. The use of an ethylene derivative as claimed in any one of claims 1 to 18, or—when appropriate—an agriculturally-acceptable salt thereof, for the control of insects and acarines. 30